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EXAMINER	
DIBRINO, MARIANNE NMN	

ART UNIT	PAPER NUMBER
1644	48

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/017,743	SETTE ET AL.	
	Examiner	Art Unit	
	DiBrino Marianne	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 November 2002 and 07 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *71, 74-76 and 79-111* is/are pending in the application.

4a) Of the above claim(s) *81,82,84-87,90,94 and 96-111* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *71,74-76,79,80,83,88,89,91-93 and 95* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *47 & 42* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/27/02 has been entered.

2. Applicant's amendments filed 11/27/02 (Paper No. 41) and 3/7/03 (Paper No. 46) are acknowledged and have been entered.

3. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. **Full compliance with the sequence rules is required in response to this Office Action. A complete response to this Office Action should include both compliance with the sequence rules and a response to the Office Action set forth below. Failure to fully comply with both these requirements in the time period set forth in this Office Action will be held non-responsive.**

4. Since Applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits.

Applicant is reminded that the elected invention is an isolated nucleic acid molecule encoding a peptide and an "other molecule", and Applicant's elected species of peptide is FPIPSSWAF (SEQ ID NO: 22) and the "other molecule" is a CTL epitope.

The species of isolated nucleic acid molecule encoding a peptide from different proteins are distinct because they encode different sequences with different amino acid residues, they are from different proteins and elicit differently-restricted immune responses to different proteins and some bear different motifs and bind different MHC molecules. The species of "other molecule" are distinct because they are different molecules that encode either HTL, mRNA stabilization sequence, or leader/signal sequence which are different sequences with different functions, i.e., for example, to elicit T cell help in the case of HTL.

Accordingly, newly submitted claims 81, 82, 84-87, 90, 94 and 96-111 (non-elected species of the claimed invention), are withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

Claims 71, 74-76, 79, 80, 83, 88, 89, 91, 92, 93 and 95 are presently being examined.

5. The disclosure is objected to because of the following informalities:

Handwritten changes were made to Figure 1 which are not initialed and dated.

Appropriate correction is required.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 71, 74-76, 79, 80, 83, 88, 89, 91, 92, 93 and 95 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The amendatory material not supported by the specification and claims as originally filed is as follows: The specification does not provide support for the claimed motif bearing peptides (i.e., Pro at position 2 and Leu, Phe, Met, Trp, Ala or Tyr at the carboxy-terminus) recited in base claim 71 binding to HLA molecules other than HLA-B3501, B5101, B5301 or B5401 (see Figure 2 and see #11 below).

8. Claims 71, 74-76, 79, 80, 83, 88, 89, 91, 92, 93 and 95 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the. . .claimed subject matter", Vas-Cath, Inc. V. Mahurkar, 19 U.S.P.Q.2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the applicant had possession at the time of invention of the claimed inventions.

The instant claims encompass nucleic acids encoding MHC binding peptides derived from a variety of antigens wherein 2 amino acids are specified. The use for the claimed nucleic acids disclosed in the specification is generation of immunogenic peptides. The specification discloses that two amino acids recited in the claim are pertinent to HLA binding of said peptides. However, the art recognizes that in order to be used for generating an immunogenic response that said peptide must bind MHC and also present an epitope recognized by T cells. The art recognizes that the T cell epitope differs from the amino acids pertinent to MHC binding. There is no written description in the specification of the amino acids that constitute the T cell epitope in the peptide recited in the claim. Therefore, the skilled artisan cannot envision the detailed structure of the encompassed peptides (and nucleic acid encoding said peptides) and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. In the instant application, the amino acid itself or isolated peptide is required. See Fiers v. Revel, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Lts., 18 USPQ2d 1016.

In view of the aforementioned problems regarding description of the claimed invention, the specification does not provide an adequate written description of the invention claimed herein. See The Regents of the University of California v. Eli Lilly and Company, 43 USPQ2d 1398, 1404-7 (Fed. Cir. 1997). In University of California v. Eli Lilly and Co., 39 U.S.P.Q.2d 1225 (Fed. Cir. 1995) the inventors claimed a genus of DNA species encoding insulin in different vertebrates or mammals, but had only described a single species of cDNA which encoded rat insulin. The court held that only the nucleic acids species described in the specification (i.e. nucleic acids encoding rat insulin) met the description requirement and that the inventors were not entitled to a claim encompassing a genus of nucleic acids encoding insulin from other vertebrates, mammals or humans, id. at 1240. The Federal Circuit has held that if an inventor is "unable to envision the detailed constitution of a gene so as to distinguish it from other materials. . .conception has not been achieved until reduction to practice has occurred", Amgen, Inc. v. Chugai Pharmaceutical Co, Ltd., 18 U.S.P.Q.2d 016 (Fed. Cir. 1991). Attention is also directed to the decision of The Regents of the University of California v. Eli Lilly and Company (CAFC, July 1997) wherein is stated: "The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 222 USPQ 369, 372-373 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. Thus, as we have previously held, a cDNA is not defined or described by the mere name "cDNA," even if accompanied by the name of the protein that it encodes, but requires a kind of specificity usually achieved by means of the recitation of the sequence of nucleotides that make up the cDNA." See Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 71, 74-76, 79, 80, 83, 88, 89, 91, 92, 93 and 95 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 71 and 83 are indefinite in the recitation of "Plasmodium falciparum" antigen because the species and genus of the said antigen should be underlined.

11. The invention is drawn to an isolated nucleic acid molecule comprising a nucleotide sequence encoding a peptide (or a peptide and a CTL epitope peptide) consisting of 9-10 amino acid residues with the motif recited in the instant claims, wherein the peptide is associated with binding to multiple HLA molecules recited in instant claim 71. With regard to application of prior art, the filing date of the instant claims is that of the instant application, i.e., 2/3/98, because the scope of the claimed invention is not disclosed in parent applications 08/590,298, 08/753,615, 08/590,298 and 08/452,843. The parent applications do not support the claimed method.

Applicant's arguments in the amendment filed 11/27/02 have been fully considered but are not persuasive.

It is the Applicant's position that the instant application is entitled to the benefit of the filing date of at least parent application serial no. 08/344,824 (11/23/94) and 08/278,634 (7/21/94) and Applicant cites a Table on page 21 of the said amendment for location of support in the two said parent applications.

It is the Examiner's position that with regard to the parent applications, the parent applications do not provide support for the motif amino acid residues at positions 2 and at the carboxy-terminus of the peptides for binding all of the recited HLA molecules in claim 71, nor for all of the recited motif amino acid residues to all of the recited HLA molecules. It is the Examiner's position that application serial no. 08/278,634 discloses *testing* peptides with the recited motif for binding to HLA molecules, that a subset of those molecules to be tested are disclosed in table 2 on page 7, that cell lines useful as source material for isolation of other HLA molecules are disclosed on page 9 in table 3, that a subset of B pocket motif amino acid residues (i.e., position 2 of the peptide) and F pocket motif amino acid residues (i.e., carboxy-terminal position of the peptide) and notably missing Alanine in any of the motifs for the carboxy-terminal amino acid residue are disclosed in Table 6, are disclosed for a subset of HLA molecules recited in the instant claims; in addition, no disclosure is made for HLA-Cw0601 in table 6 on page 33, table 8 on page 37 discloses a comparison of B pocket residues of A3-like HLA alleles, table 9 on page 38 discloses position 2 proline and carboxy-terminal

position phenylalanine for binding of peptides to HLA-B54, and table 10 on page 39 discloses a comparison of B pocket residues of alleles preferring peptides with proline at position 2.

It is the Examiner's further position that application serial no. 08/344,824 (filed 11/23/94) does not provide support for the same reasons that 08/278,634 does not. For instance, 08/344,824 discloses (on page 3 at lines 11-14) that Table 6 on page 33 discloses Position 2 Pro and certain subsets of, but not all of, the C-terminal hydrophobic residues (and excluding the amino acid residue Ala, or "A") recited in the instant claims for certain HLA alleles (for example, LIVYFW for HLA-B7, LIV for HLA-B51, LIVMYFW for HLA-B53 and HLA-Cw6).

Therefore, the motif recited in the instant claims for peptides of 9 or 10 amino acid residues in length having the said motif to the HLA molecules recited in the instant claim 71 is not supported by 08/344,824.

It is also the Examiner's position that the 08/452,843 (5/30/95), 08/753,615 (11/27/96) and 08/590,298 (1/23/096) parent applications do not provide support for same reasons that the 08/278,634 and 08/344,824 applications do not.

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

13. Claims 71, 74-76, 80, 92, 93 and 95 are rejected under 35 U.S.C. 102(b) as being anticipated by Mancini et al (J. Biotechnology, vol. 44, 1996, pages 47-57) as evidenced by admissions in the specification on page 5 at lines 6-11 and on pages 28-31 (Tables 5-6).

Mancini et al teach isolated nucleic acid molecules encoding HBV surface antigens, i.e., env proteins, and comprising T cell epitopes (including CTL epitopes). It is an inherent property of the art molecules that they comprise a nucleotide sequence encoding at least a first peptide consisting of 9 to 10 amino acid residues with Pro at position 2 and Phe at position 9, wherein the first encoded peptide binds to at least two or three or more than three of the HLA molecules recited in instant claim 71, and wherein the said molecules further encode a second peptide which is a T cell epitope.

The admissions in the specification on page 5 at lines 6-11 and on pages 28-31 (Tables 5-6) are that immunogenic peptides are identified in suitable antigens such as HBV core and surface antigens using a scan for subsequences bearing a supermotif, and the Tables list peptides from HBV and other antigens that contain subsequences including peptide IPIPSSWAF (HBV env 313) that bear a supermotif of Pro at position 2 and Phe at position 9.

Therefore, the claimed isolated nucleic acid molecule appears to be the same or similar to the isolated nucleic acid molecule of the prior art absent a showing of unobvious differences. Since the Patent Office does not have the facilities for examining and comparing the process of the instant invention to those of the prior art, the burden is on applicant to show an unobvious distinction between the process of the instant invention and that of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

14. Claims 71, 74, 75, 83, 92 and 93 are rejected under 35 U.S.C. 102(e) as being anticipated by US 6,419,931 B1 as evidenced by Rammensee et al (Immunogenetics, Vol. 41, pages 178-228, 1995, of record) and Hill et al (Nature 360, 1992, 434-439).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

US 6,419,931 B1 discloses the peptide from P. falciparum KPIVQYDNF is a CTL epitope and further discloses an isolated nucleic acid molecule encoding the said peptide (especially Table spanning columns 9 and 10, and column 19 at lines 22-35).

Evidentiary reference Rammensee et al teach a peptide with the sequence KPIVQYDNF which is a T cell epitope corresponding to amino acid residues 1786-1794 of P. falciparum LSA (especially page 207, Table 3) that binds to HLA-B53.

Evidentiary reference Hill et al teach the same peptide taught by Rammensee et al, KPIVQYDNF which is a T cell epitope that binds to HLA-B53 corresponding to amino acid residues 1786-1794 of P. falciparum LSA. Hill et al further teach that use of the peptide as a malaria vaccine component.

Since the plasmodium peptide taught by Rammensee et al and Hill et al binds to HLA-B53 and has anchor amino acid residues at anchor positions (bolded in Table 3 of Rammensee et al), it is an inherent property that the said peptide would bind to several if not all of the HLA molecules listed in instant claim.

Therefore, the claimed isolated nucleic acid molecule appears to be the same or similar to the isolated nucleic acid molecules of the prior art absent a showing of unobvious differences. Since the Patent Office does not have the facilities for examining and comparing the process of the instant invention to those of the prior art, the burden is on applicant to show an unobvious distinction between the process of the instant invention and that of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

15. Claims 71, 74, 75, 79, 88 and 89 are rejected under 35 U.S.C. 102(e) as being anticipated by US 5,610,067 as evidenced by as evidenced by Rammensee et al (Immunogenetics, Vol. 41, pages 178-228, 1995, of record) and admissions in the specification on page 5 at lines 6-11.

US 5,610,067 discloses isolated nucleic acid molecules encoding HIV nef protein. It is an inherent property of the art molecules that they comprise a nucleotide sequence encoding at least a first peptide consisting of 9 to 10 amino acid residues with Pro at position 2 and Leu at the carboxy terminal position, wherein the first encoded peptide binds to at least two or three or more than three of the HLA molecules recited in instant claim 71.

Evidentiary reference Rammensee et al teach a peptide with the sequence TPGPGVRYPL which is a T cell epitope corresponding to amino acid residues 128-137 of HIV nef viral protein and which binds to HLA-B7 (especially page 197, last sequence in Table 3).

The admissions in the specification on page 5 at lines 6-11 and on pages 28-31 (Tables 5-6) are that immunogenic peptides are identified in suitable antigens such as HIV antigens using a scan for subsequences bearing a supermotif.

Since the peptide taught by Rammensee et al binds to HLA-B7 and has anchor amino acid residues at anchor positions (bolded in Table 3 of Rammensee et al), it is expected that the said peptide would bind to several if not all of the HLA molecules listed in instant claim.

16. Claims 71, 74, 75, 79, 88 and 89 are rejected under 35 U.S.C. 102(a) as being anticipated by US 5,610,067 as evidenced by as evidenced by Rammensee et al (Immunogenetics, Vol. 41, pages 178-228, 1995, of record) and admissions in the specification on page 5 at lines 6-11.

US 5,610,067 discloses isolated nucleic acid molecules encoding HIV nef protein. It is an inherent property of the art molecules that they comprise a nucleotide sequence encoding at least a first peptide consisting of 9 to 10 amino acid residues with Pro at position 2 and Leu at the carboxy terminal position, wherein the first encoded peptide binds to at least two or three or more than three of the HLA molecules recited in instant claim 71.

Evidentiary reference Rammensee et al teach a peptide with the sequence TPGPGVRYPL which is a T cell epitope corresponding to amino acid residues 128-137 of HIV nef viral protein and which binds to HLA-B7 (especially page 197, last sequence in Table 3).

The admissions in the specification on page 5 at lines 6-11 and on pages 28-31 (Tables 5-6) are that immunogenic peptides are identified in suitable antigens such as HIV antigens using a scan for subsequences bearing a supermotif.

Since the peptide taught by Rammensee et al binds to HLA-B7 and has anchor amino acid residues at anchor positions (bolded in Table 3 of Rammensee et al), it is expected that the said peptide would bind to several if not all of the HLA molecules listed in instant claim.

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

18. Claims 71, 74-76, 80, 92, 93 and 95 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Sidney et al (J. Immunol. Vol. 157, 1996, pages 3480-3490, of record) in view of WO 93/03764 (of record).

Sidney et al teach an 'anchor fixed' nonamer peptide with the sequence FPIPSSWAF that was altered at position 1 in the base peptide IPIPSSWAF (HBV env 313), said base peptide being derived from the hepatitis B virus envelope protein (especially Table VI and Discussion section on pages 4388-3489). Sidney et al teach that the peptide FPIPSSWAF binds an HLA molecule at IC_{50} values ranging from 105 nM to 1.2 nM and binds with higher affinity than the base peptide IPIPSSWAF (especially Table VI). Said peptide has Pro at position 2 and Phe at position 9 and is associated with binding to multiple HLA molecules, four of which are HLA molecules recited in instant claim 71 (especially Table VI of the reference).

Sidney et al do not teach an isolated nucleic acid encoding a peptide comprising FPIPSSWAF, nor a nucleic acid molecule encoding the said peptide and another peptide that is a CTL epitope.

WO 93/03764 teaches peptides from hepatitis B virus (HBV) that stimulate CTL are useful in diagnostic methods (especially Abstract and page 23, lines 25-31). WO 93/03764 further teaches that peptides of the invention can be synthesized chemically or by recombinant DNA technology wherein a nucleotide sequence which encodes said peptide, or a heteropolymer comprising said peptide in fusion with another peptide that is a CTL epitope, is inserted into an expression vector, transformed or transfected into an appropriate host cell and cultivated under conditions suitable for expression (especially page 22, lines 6-33, page 23, lines 3-24 and page 31, lines 13-23). WO 93/03764 teaches a DNA construct encoding a peptide (especially claim 59) that is used for the expression of said peptide.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have made an isolated nucleic acid molecule encoding the peptide FPIPSSWAF of Sidney et al because Sidney et al teach said HBV-derived peptide is immunogenic and WO 93/03764 teaches nucleic acids encoding immunogenic HBV-derived peptides. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have made an isolated nucleic acid molecule encoding the peptide FPIPSSWAF of Sidney and further encoding a peptide which is a CTL epitope because WO 93/03764 further teaches that peptides of the invention can be synthesized chemically or by recombinant DNA technology, wherein a nucleotide sequence which encodes a heteropolymer comprising said peptide is in fusion with another peptide that is a CTL epitope.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to produce the peptide FPIPSSWAF of Sidney et al, or larger peptides comprising said peptide, for use in diagnostic assays as taught by WO 93/03764 or to stimulate CTL which could be used in diagnostic assays.

Applicant's arguments in the amendment filed 11/27/02 have been fully considered but are not persuasive.

It is Applicant's position that Sidney et al is not available as prior art against the instant claims and WO 93/03764 does not teach nor suggest the claimed isolated nucleic acid molecule.

It is the Examiner's position that Sidney et al is available as prior art because the instant claims are entitled to a priority date of 2/3/98 as enunciated supra.

19. Claims 71, 74-76, 79, 80, 83, 88, 89, 91, 92, 93 and 95 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Rammensee et al (Immunogenetics, Vol. 41, pages 178-228, 1995, of record) in view of EP 0346022A1 (of record) and Hill et al (Nature 360, 1992, 434-439).

Rammensee et al teach a peptide with the sequence TPGPGVRYPL which is a T cell epitope corresponding to amino acid residues 128-137 of HIV nef viral protein and which binds to HLA-B7 (especially page 197, last sequence in Table 3). Rammensee et al also teach a peptide with the sequence KPIVQYDNF which is a T cell epitope corresponding to amino acid residues 1786-1794 of P. falciparum LSA (especially page 207, Table 3) which binds to HLA-B53.

Rammensee et al do not teach an isolated nucleic acid encoding a peptide comprising TPGPGVRYPL, nor KPIVQYDNF, nor a nucleic acid molecule encoding either of the said peptides and another peptide that is a CTL epitope. Rammensee et al also teach that peptides that bind to class I molecules that are 9 or 10 amino acid residues in length.

EP 0346022A1 teaches peptides from the infectious agent HIV viral proteins that bind HLA class I molecules and that can be used for diagnostic purposes (especially Abstract). EP 0346022A1 further teaches that the vaccine may comprise more than one peptide that can stimulate a CTL response, the said peptides can be used to construct synthetic or fusion proteins that contain the relevant peptide epitopes, and the peptide or fusion protein can be made using known DNA techniques (especially page 2 at lines 39-46). EP 0346022A1 teaches CTL epitopes in peptides of up to 15 amino acid residues in length (especially page 2 at lines 23-25).

Hill et al teach the same peptide taught by Rammensee et al, KPIVQYDNF which is a T cell epitope that binds to HLA-B53 corresponding to amino acid residues 1786-1794 of P. falciparum LSA. Hill et al further teach that use of the peptide as a malaria vaccine component.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have made an isolated nucleic acid molecule encoding the peptide TPGPGVRYPL of Rammensee et al or the peptide KPIVQYDNF of Rammensee et al and Hill et al alone or in a fusion protein with another CTL epitope, or to make an isolated nucleic acid molecule encoding a fusion protein of the peptide with another CTL epitope peptide, because Rammensee et al teach that the said peptides are CTL epitopes from HIV nef viral protein or from the malarial plasmodium falciparum LSA protein, and EP 0346022A1 teaches that the said HIV-derived peptides that are CTL epitopes are useful for diagnostic purposes, and further that the said peptides or fusion protein can be made using known DNA techniques, and Hill et al teach that the CTL epitope peptide from LSA protein is useful as a vaccine component to treat malaria.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to produce the peptide TPGPGVRYPL taught by Rammensee et al, or larger peptides comprising said peptide and another T cell epitope, for diagnostic purposes as taught by EP 0346022A1,or to stimulate CTL which could be used in diagnostic assays. In addition, because the peptide taught by Rammensee et al binds to HLA-B7 and has anchor amino acid residues at anchor positions (bolded in Table 3 of Rammensee et al), it is expected that the said peptide would bind to several if not all of the HLA molecules listed in instant claim. One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to produce the peptide taught by Rammensee et al and Hill et al KPIVQYDNF or larger peptides comprising said peptide and another T cell epitope, for diagnostic purposes as taught by EP 0346022A1 for another infectious agent, or to stimulate CTL which could be used in diagnostic assays for use as a vaccine as taught by Hill et al for treatment of the infectious agent causing malaria. In addition, because the peptide taught by Rammensee et al and Hill et al binds to HLA-B53 and has anchor amino acid residues at anchor positions (bolded in Table 3 of Rammensee et al), it is expected that the said peptide would bind to several if not all of the HLA molecules listed in instant claim.

20. No claim is allowed.

21. It is noted by the Examiner that instant claim 71 has a typographical error at line 2. A space should be present between "of" and "9".

22. The references crossed out in Applicant's IDS filed 11/27/02 have not been considered because they cannot be located in the parent applications. They will be considered in the next Office Action. It would expedite prosecution if Applicant would send in copies of the references.

23. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 703-308-0061. The examiner can normally be reached on Monday, Wednesday and Friday afternoons.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached on (703) 308-3973. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.
Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

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June 16, 2003

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